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| 10/518,496 | 09/19/2005 | Maria Prat Quinones | 09605.0007 | 4930 |

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| EXAMINER |
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RAHMANI, NILOOFAR

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| ART UNIT | PAPER NUMBER |
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1625

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12/07/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/518,496

Applicant(s)

PRAT QUINONES ET AL.

Examiner

Niloofar Rahmani

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 36-69 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 36-69 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☒ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 36-69 are pending in the instant application and claims 1-35 are cancelled.

2. ***Priority***

This application was filed on 09/19/2005, which is a 371 of PCT/EP03/06472, filed on 06/18/2003, which claims benefit of priority document SPAIN P200201439, filed on 06/21/2002. The claimed benefit of priority date is denied. There is no certified translation of the priority document. The filing date of the instant application is 06/18/2003.

3. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 65 is rejected because the claim is vague and indefinite. What are they claiming? Do the applicants claim the compound claim or the method of using the compound? Correction is required.

4. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 65-69 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification does not enable the instant compound to alter the gene expression and therefore to treat any and all known or unknown diseases. The claim contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

- 1) The breadth of the claims.
- 2) The nature of the invention,
- 3) The state of the prior art,
- 4) The level of one of ordinary skill,

- 5) The level of predictability in the art,
- 6) The amount of direction provided by the inventor,
- 7) The existence of working examples,
- 8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The instant invention is drawn to method for treating a subject afflicted with a pathological condition or disease susceptible to amelioration by antagonism of M3 muscarinic receptors using the compounds of claim 36.

The state of the prior art: " Acetylcholine (Ach) plays an important role in smooth muscle contraction and in the development of airway narrowing; preliminary evidences led us to hypothesize that Ach might also play a role in the development of airways inflammation in chronic obstructive pulmonary disease(COPD). The results obtained show that muscarinic receptors may be involved in airway inflammation in COPD subjects through Ach-induced, ERK1/2-dependent LTB4 release. Muscarinic antagonism may contribute to reduce neutrophil infiltration and activation in COPD."(Profita et al., Allergy, 2005, Vol. 60, pages 1361-1369.)

The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seeming high level of skill in the art. The

existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects, whether or not the compounds of formula of claim 1 would be used for preventing or treating a disease for which gene expression control is effective.

Amount of guidance/working examples: On pages 30-33 of the specification, applicants have shown that the nexus between the instant compounds and muscarinic receptor. However, applicant provides no guidance or examples for how muscarinic receptor could treat any and all known or unknown diseases. There are no examples in the instant specification showing that the instant compounds can treat any diseases from respiratory, urological, and gastrointestinal disease or disorder.

The breadth of the claims: The breadth of claims is drawn to method for treating a subject afflicted with a pathological condition or disease susceptible to

amelioration by antagonism of M3 muscarinic receptors using the compounds of claim 36.

The quantity of undue experimentation needed: Since the guidance and teaching provided by the specification is insufficient for treating diseases by antagonism of M3 muscarinic receptor is effective, one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Taking all of the above into consideration, it is not seen where the instant claim 65-69, for treating diseases by antagonism of M3 muscarinic receptor is effective, have been enabled by the instant specification.

5. *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 36-64 are rejected under 35 U.S.C. 102(a,e) as being anticipated by Catena Ruiz et al. WO 03/053966. Catena Ruiz et al. disclosed the instant claimed compounds on pages 23-37, Examples 1-71. Therefore, the instant claim is anticipated by Catena Ruiz et al.

6. Claims 36-64 are rejected under 35 U.S.C. 102(a,e) as being anticipated by Buil Albero et al. WO 02/051841. Buil Albero et al. disclosed the instant claimed compounds on pages 22-53, Examples 1-160. Therefore, the instant claim is anticipated by Buil Albero et al.

7. Claims 36-64 are rejected under 35 U.S.C. 102(b) as being anticipated by Farrerons Gallemi et al. WO 02/00652. Farrerons Gallemi et al. disclosed the instant claimed compounds on pages 12-21, Examples 1-69. Therefore, the instant claim is anticipated by Farrerons Gallemi et al.

8. *Claim Rejections - Obvious Double Patenting*

Claims 36-64 is rejected under the judicially created doctrine obviousness-type double patenting as being unpatentable over the claims 1-19 of the Buil Albero et al. US 7208501. Although the conflicting claims are not identical, they are not patentably distinct from each other because the current invention embraces the invention claimed in the above patent.

Determination of the scope and content of the prior art (MPEP §2141.01)

Buil Albero et al. claimed identical compounds and salt of the compounds in claims 1-19 as the instant claims 36-64.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the issued claims is the claims are not word for word identical but the scope of both sets of claims overlaps mostly significantly with each other.

Finding of prima facie obviousness-rational and motivation (MPEP §2142.2143)

The issued claims 1-19 of US 7208501 are therefore fully embraced by the instant claims 36-64.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment

by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 168 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130 (b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).
NILOOFAR RAHMANI


MARGARET SEAMAN

11/29/2007

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PRIMARY EXAMINER

GROUP 1625